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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/914,615	12/26/2001	Paul Meers		9551

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EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT PAPER NUMBER

1615

DATE MAILED: 03/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/914,615

Applicant(s)

MEERS ET AL.

Examiner

Gollamudi S. Kishore, Ph.D

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-7 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____.  |

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### DETAILED ACTION

The amendment dated 12-5-05 is acknowledged.

Claims included in the prosecution are 1-7.

#### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim (5,723,147) cited in the previous action in combination with either Gao (5,795,587) or Papahadjopoulos (6,071,533).

Instant method claims are drawn to formation of liposomes wherein the active agent is complexed with a complexing agent; the method steps in claims 1 and 2 recite two variables. 1) the complexing agent is added in the second aqueous solution whereas the active agent is added in the first aqueous phase (claim 1); 2) the complexing agent is added in the first aqueous medium and the active agent is added in the second aqueous medium.

Kim (587) discloses a process of preparation of liposomes in which the lipid in an organic solvent is added with an aqueous solution of an active agent, which in turn is added, with a second aqueous solution containing a cationic amino acid lysine. The organic solvent is then removed. Kim teaches various active agents including DNA and RNA (abstract, col. 6, line 62 and Examples). What are lacking in Kim are the teachings of adding a complexing agent such as polylysine or spermine or spermidine.

Similarly, Kim (cancer research) discloses a process of preparation of liposomes in which the lipid in an organic solvent is added with an aqueous solution of an active agent, which in turn is added, with a second aqueous solution containing cationic amino acid lysine. The organic solvent is then removed (Materials and Methods section on col. 2, page 1596).

Gao teaches liposomal delivery systems in which the nucleic acid is complexed with a polycation. According to Gao such complexes are stable, capable of being produced at relatively high concentrations and retain the biological activity of the drug component over time in storage. Such liposomes have high transfection ability. The polycations include polylysine, spermine and spermidine (abstract, col. 4, line 66 through col. 5, line 8, col. 9, lines 40-55 and examples).

Papahadjopoulos discloses liposomal delivery system in which nucleic acid is complexed with a polycation such as spermidine, spermine and poly amino acids. According to Papahadjopoulos, surprising discovery of their invention is that the use of polycation provides a lipid-nucleic acid complex that remains capable of transfecting a

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cell in vivo even after a period of prolonged storage (abstract, col. 7, lines 9-40, col. 8, lines 20-28).

The addition of an aqueous solution containing a polycation such as polylysine or spermine or spermidine to the organic solvent-aqueous solution mixture containing an active agent such as a nucleic acid would have been obvious to one of ordinary skill in the art since the references of Gao, and Papahadjopoulos teach that the complex formed has a high transfection ability even after prolonged storage. Although Kim does not teach the formation of the emulsion first with the complexing agent and then the addition of the active agent, it would have been obvious to one of ordinary skill in the art that a complex formation would occur whether the active agent is added to the complexing agent emulsion or complexing agent is added to the active agent containing emulsion since the complexation process is between an anionic agent and a cationic agent.

Applicant's arguments have been fully considered, but are deemed to be moot in view of the new rejections based on the amendments.

The reference of Stadler (5,286,634) which teaches synergistic combination of DNA and polycations is cited of interest.

1. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Gollamudi S Kishore, Ph.D  
Primary Examiner  
Art Unit 1615

GSK